



10/14
Docket No. 0575/63711-A/JPW/GJG/AX

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Virginia W. Cornish
Serial No. : 10/056,874
Filed : January 24, 2002
For : COVALENT CHEMICAL INDUCERS OF PROTEIN DIMERIZATION AND THEIR USES IN HIGH THROUGHPUT BINDING SCREENS

1185 Avenue of the Americas
New York, New York 10036
May 3, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicant would like to direct the Examiner's attention to the following disclosures, which are listed on Form PTO-1449 (**Exhibit A**). Copies of the disclosures listed below as items 1-39 are attached hereto as **Exhibits 1-42**, respectively:

- . U.S. Patent No. 5,928,868 (Liu et al.) issued July 27, 1999 (**Exhibit 1**);
- . U.S. Patent No. 5,736,843 (Landry) issued April 7, 1998 (**Exhibit 2**);
- . U.S. Patent No. 5,468,614 (Fields et al.) issued November 21, 1995 (**Exhibit 3**);

Virginia W. Cornish
U.S. Serial No.: 10 056,874
Filed: January 24, 2002
Page 2

- . U.S. Patent No. 5,314,817 (Schultz, P.) issued May 24, 1994
Exhibit 4);
- . U.S. Patent No. 5,194,594 (Kwawli et al.) issued March 16, 1993 (**Exhibit 5);**
- . PCT International Application Publication No. WO 01/53355 (Cornish et al.) published July 26, 2001 (**Exhibit 6);**
- . PCT International Application Publication No. WO 99/10510 (Natesan et al.) published March 4, 1999 (**Exhibit 7);**
- . PCT International Application Publication No. WO 99/10508 (Natesan et al.) published March 4, 1999 (**Exhibit 8);**
- . PCT International Application Publication No. WO 98/13353 (Whitney et al.) published April 2, 1998 (**Exhibit 9);**
- . PCT International Application Publication No. WO 97/31113 (Rickles et al.) published August 28, 1997 (**Exhibit 10);**
- . PCT International Application Publication No. WO 96/30540 (Visien et al.) published October 3, 1995 (**Exhibit 11);**
- . European Patent Application Publication No. EP 0 742 015 (Kadow et al.), published November 13, 1996 (**Exhibit 12);**
- . Austin DJ, et al. Proximity versus allosteric: the role of regulated protein dimerization in biology. 1994. Chem Biol.

Virginia W. Cornish
U.S. Serial No.: 10/056,874
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Page 3

103 : 131-6 (**Exhibit 13**) ;

14. Beishaw PJ, et al. Controlling protein association and subcellular localization with a synthetic ligand that induces heterodimerization of proteins. 1996. Proc. Natl Acad Sci USA 93(10):4604-7 (**Exhibit 14**) ;
15. Beishaw PJ, et al. Controlling programmed cell death with a cyclophilin-cyclosporin-based chemical inducer of dimerization. 1996. Chem. Biol. 3:731-738 (**Exhibit 15**) ;
16. Choi J, et al. Structure of the FKBP-12-Rapamycin complex interacting with the binding domain of human FRAF. 1996. Science 273(5272):239-42 (**Exhibit 16**) ;
17. DeGrado WF, et al. Screening, selection and design: standing at the crossroads in three dimensions. 1997. Current Opinion in Structural Biology 7:455-456 (**Exhibit 17**) ;
18. Diver SR, et al. Single-step synthesis of cell-permeable protein dimerizers that activate signal transduction and gene expression. 1997. J. Am. Chem. Soc. 119, 5106-5109 (**Exhibit 18**) ;
19. Ho SN, et al. Dimeric ligands define a role for transcriptional activation domains in reinitiation. 1996. Nature. 382(6594):822-6 (**Exhibit 19**) ;

Virginia W. Cornish
U.S. Serial No.: 10 056,874
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Page 4

- Holsinger LJ, et al. Signal transduction in T lymphocytes using a conditional allele of Sos. 1995. Proc. Natl. Acad. Sci. USA 92:9810-9814 (**Exhibit 20**);
21. Hung DT, et al. Understanding and controlling the cell cycle with natural products. 1996. Chem. Biol. 3:623-639 (**Exhibit 21**);
22. Klemm JD, et al. Dimerization as a regulatory mechanism in signal transduction. 1998. Annu. Rev. Immunol. 16:569-92 (**Exhibit 22**);
23. Liberles SD, et al. Inducible gene expression and protein translocation using nontoxic ligands identified by a mammalian three-hybrid screen. 1997. Proc. Natl. Acad. Sci. USA 94(15):7825-7830 (**Exhibit 23**);
24. Licitra EJ, et al. A three-hybrid system for detecting small ligand-protein receptor interactions. 1996. Proc. Natl. Acad. Sci. USA 93:12817-12821 (**Exhibit 24**);
25. Pedersen H, et al. A method for directed evolution and functional cloning of enzymes. 1998. Proc. Natl. Acad. Sci. USA 95:10523-10528 (**Exhibit 25**);
26. Prusky MN, et al. Mechanistic studies of a signaling pathway activated by the organic dimerizer FK1012. 1994. Chem. Biol. 1:163-172 (**Exhibit 26**);

Virginia W. Cornish
U.S. Serial No.: 10/056,874
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Page 5

27. Schreiber SL. Chemical genetics resulting from a passion for synthetic organic chemistry. 1998. *Bioorganic & Medicinal Chemistry* 6:1127-1152 (**Exhibit 27**);
28. Spencer DM, et al. Controlling signal transduction with synthetic ligands. 1993. *Science* 262(5136):1019-1024 (**Exhibit 28**);
29. Spencer DM, et al. Functional analysis of Fas signaling in vivo using synthetic inducers of dimerization. 1996. *Curr Biol.* 6(7):839-47 (**Exhibit 29**);
30. Spencer DM, et al. A general strategy for producing conditional alleles of Src-like tyrosine kinases. 1995. *Proc. Natl. Acad. Sci.* 92:9805-9809 (**Exhibit 30**);
31. Stockwell BR, et al. TGF-beta-signaling with small molecule FKBP12 antagonists that bind myristoylated FKBP12-TGF-beta type 1 receptor fusion proteins. 1998. *Chem Biol.* 5(7):385-95 (**Exhibit 31**);
32. Stockwell BR, et al. Probing the role of homomeric and heteromeric receptor interactions in TGF-beta signaling using small molecule dimerizers. 1998. *Curr Biol* 8(13):761-766 (**Exhibit 32**);
33. Winkler T, et al. Confocal fluorescence coincidence analysis: An approach to ultra high-throughput screening. 1998. *Proc. Natl. Acad. Sci. USA* 96:1375-1378 (**Exhibit 33**);

Virginia W. Cornish
U.S. Serial No.: 10/056,874
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Page 6

- 4. Yang J, et al. Small-molecule control of insulin and PDGF receptor signaling and the role of membrane attachment. 1997. Curr. Biol. 8:11-18 (**Exhibit 34**) ;
- 5. Zlokarnik G, et al. Quatitation of tranmscription and clonal selection of single living cells with beta-lactamase as reporter. 1998. Science 279(5347) :84-8 (**Exhibit 35**) ;
- 6. Search Report dated May 14, 2001 corresponding PCT International Application No. PCT/US01/02285 (**Exhibit 36**) ;
- 7. Lin, H., et al. Dexamethasone-Methotrexate: An Efficient Chemical Inducer of Protein Dimerization *In Vivo*. 2000. J.Am.Chem.Soc. 122:4247-4248 (**Exhibit 37**) ;
- 8. Kopytek, S.J., et al. Chemically Induced Dimerization of Dihydrofolate Reductase by a Homobifunctional Dimer of Methotrexate. 2000. Chem Biol. 7:313-321 (**Exhibit 38**) ;
- 9. U.S. Serial No. 09/768,479, filed January 24, 2001 (**Exhibit 39**) ;
- 10. Firestone, S.M., et al. Using an AraC-Based three-hybrid system to detect biocatalysts in vivo. 2000. Nature Biotechnology. 18, 544-547 (**Exhibit 40**) ;
- 11. Pailetier, J.N., et al. Oligomerization domain-directed reassembly of active dihydrofolate reductase from rationally designed fragments. 1998.

Virginia W Cornish
U.S. Serial No.: 10/056,874
Filed: January 24, 2002
Page 7

Proc.Natl.Acad.Sci.USA. 95, 12141-12146 (**Exhibit 41**); and

42. Ladant, D., Karimova, G. Genetic systems for analyzing protein-protein interactions in bacteria. 2000. Res. Microbiol. 151, 711-720 (**Exhibit 42**).

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. If any such fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

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Reg. No. 28,678
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Form PTO-1449

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Patent and Trademark OfficeAtty. Docket No.
63711-A JPW/GJGSerial No.
10'056,874Applicant
Virginia W. CornishFiling Date
January 24, 2002Group
1614

INFORMATION DISCLOSURE STATEMENT

(Use several sheets if necessary)

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number							Date	Name	Class	Subclass	Filing Date if Appropriate	
	5	9	2	8	8	6	8						
	5	9	2	8	8	6	8	Jul 27, 1999	Liu et al.				
	5	7	3	6	3	4	3	April 7, 1998	Landry				
	5	4	6	8	6	1	4	Nov. 21, 1995	Fields et al.				
	5	3	1	4	8	1	7	May 24, 1994	Schultz, P.				
	5	1	9	4	5	9	4	March 16, 1993	Kwawli et al.				
Document Number							Date	Country		Class	Subclass	Translation	
	0	1	5	3	3	5	5	Jul 26, 2001	WO			Yes	No
	9	9	1	0	5	1	0	March 4, 1999	WO				
	9	9	1	0	5	0	8	March 4, 1999	WO				
	9	8	1	3	3	5	3	April 2, 1998	WO				
	9	7	3	1	1	1	3	August 28, 1997	WO				
	9	6	3	0	5	4	0	October 3, 1999	WO				
	0	7	4	2	0	1	5	November 13, 1996	EP				
	Austin DJ, et al. Proximity versus allostery: the role of regulated protein dimerization in biology. 1994. Chem Biol. 1(3): 131-6 (Exhibit 13)												
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EXAMINER				DATE CONSIDERED									
*EXAMINER: Initial if reference reconsidered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.													

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 U.S. Serial No.: 10'056,874
 Filed: January 24, 2002
 Group Art Unit: 1614

Exhibit A

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O P E R A T I O N S

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Form PTO-149

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63711-A JPW GJG	10 056,874

Applicant
Virginia W. Cornish

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January 24, 2002	1614

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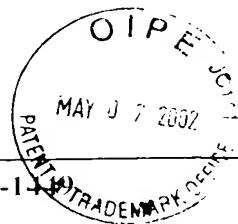
FOREIGN PATENT DOCUMENTS

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	Belshaw PJ, et al. Controlling programmed cell death with a cyclophilin-cyclosporin-based chemical inducer of dimerization. 1996. Chem. Biol. 3:731-738 (Exhibit 15)						

	Choi J, et al. Structure of the FKBP-12-Rapamycin complex interacting with the binding domain of human FRAP. 1996. Science 273(5272):239-42 (Exhibit 16)
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						Yes	No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Ho SN, et al. Dimeric ligands define a role for transcriptional activation domains in reinitiation. 1996. Nature. 382(6594):822-6 (Exhibit 19)
	Holsinger LJ, et al. Signal transduction in T lymphocytes using a conditional allele of Sos. 1995. Proc. Natl. Acad. Sci. USA 92:9810-9814 (Exhibit 20)
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